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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,928	05/05/2006	Yechezkel Barenholz	BARENHOLZ13	4078

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,928	BARENHOLZ ET AL.	
	Examiner	Art Unit	
	EMILY M. LE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/15/2005, 05/05/06, 06/30/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *76-116 and 118-127* is/are pending in the application.

4a) Of the above claim(s) *76-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *108-116 and 118-127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/15/08+06/30/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, a product, in the reply filed on 06/30/2009 is acknowledged. The traversal is on the ground(s) that the unity of inventions exists because the inventions have a shared special technical feature. In supporting the argument, Applicant notes that the special technical feature shared among the invention is the combination of the sphingoid-polyalkylamine conjugate with a biologically active molecule. This is not found persuasive because this shared technical feature fails to provide a contribution over the prior art, as evidenced by Jorgensen et al. Jorgensen et al. discloses a ceramide-polyalkylamine conjugate with a biologically active molecule. [Entire reference, including page 3, in particular.] In the absence of a contribution over the prior art, the noted shared technical feature is not a shared special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

2. Claims 1-75, 117 and 128-134 are cancelled. Claims 76-116 and 118-127 are pending. Claims 76-107 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/30/2009. Claims 108-116 and 118-127 are under examination.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 118-127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 118, which claims 119-127 depend, recites a dependency to cancelled claim 33. For the purpose of examination, claim 118 is interpreted to recite a dependency to independent claim 108.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 108-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen et al.[1]

The claims are directed toward a composition comprising a sphingoid-polyalkylamine conjugate and a biologically active molecule. Claim 109, which depends on claim 108, requires that the biologically active molecule be effective to stimulate or enhance the immune response of said subject. Claim 110, which depends on claim 109, requires that the composition to further comprise an immunostimulating agent.

Claim 111, which depends on claim 108, requires that the conjugate comprise a sphingoid backbone carrying, vial a carbamoyl bond and at least one polyalkylamine chain. Claim 112, which depends on claim 111, requires the sphingoid backbone be selected from the group consisting of ceramide, dihydroceramide, phytoceramide, dihydrophytoceramide, ceramine, dihydrocramine, phytoceramine, and dihydrophytoceramine. Claim 113, which depends on claim 112, limits the sphingoid to ceramide. Claim 114, which depends on claim 108, requires that the polyalkylamine chain be spermine, spermidine or polyalkylamine analog of spermine or spermidine.

Jorgensen et al. teaches a composition comprising a lipid-polyalkylamine conjugate. [Entire reference, in particular.] The lipid that Jorgensen et al. teaches is ceramide. [Paragraph 064, in particular.] The polyalkylamine that Jorgensen et al. teaches includes spermine and spermidine. [Paragraph 0053, in particular.] Jorgensen et al. also teaches that the lipid-polyalkylamine conjugate can be linked using a hydrocarbyl group, including carbamoyl. [Paragraphs 0047 and 0066, in particular.] In the instant case, Jorgensen et al. teaches the claimed sphingoid-polyalkylamine conjugate.

Jorgensen et al. did not include a biologically active molecule with the composition. However, Jorgensen et al. teaches that the compound is a cationic liposome that can be used to facilitate delivery of therapeutic agents such as DNA, mRNA, antisense oligonucleotides, proteins and drugs into cells—all of which are biologically active molecules that modulates and induces the immune response. [Page

[1] Jorgensen et al. U.S. PreGrant Pub. No. 2002/0188023 A1, published December 12, 2002.

1, in particular.] Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to include a biologically active molecule with the lipid-polyalkylamine conjugate of Jorgensen et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate delivery of molecules. One of ordinary skill in the art would have had a reasonable expectation of success for doing so because Jorgensen et al. discloses that lipid-polyalkylamine conjugates are effective to facilitate delivery of drugs into cells.

Additionally, it would have been prima facie obvious for one of ordinary skill in the art to also include an immunostimulating agent, such as an adjuvant to the composition rendered obvious by Jorgensen et al. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to stimulate the immune response induced by the composition rendered obvious by Jorgensen et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the use of adjuvants with therapeutic agents such as biologically active molecules is routinely practiced in the art.

7. Claims 108-116 and 118-127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al.,[2] in view of Jorgensen et al.[3]

The significance of claims 108-114 are provided above. Claim 115, which depends on claim 108, requires that the sphingoid-polyalkylamine conjugate be N-palmitoyl D-erythoro sphingosyl carbamoyl-spermine (CCS). Claim 116, which depends on claim 115, requires the biologically active molecule be derived from influenza virus or

[2] Miller et al. WO 97/45442, published December 4, 1997.

is an analog of a molecule derived from influenza virus. Claim 118, which is interpreted as depending on claim 108, specifies the broad structure for the sphingoid-polyalkylamine conjugate. Claims 119-127, which depends on claim 118, are directed to defining the various variables set forth in the structure provided in claim 118, wherein CCS encompasses the defined variables set forth therein.

CCS has the following structure:

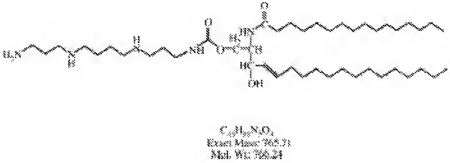

Fig. 1. *N*-palmitoyl D-erythro-sphingosyl-1-O-carbamoyl-spermine, CCS.

Miller et al. teaches a composition comprising a lipid-polyalkylamine conjugate. [Entire reference, in particular.] [Figure 5, in particular.] The lipid that Miller et al. teaches is cholesterol. The polyalkylamine that Miller et al. teaches includes spermine and spermidine and its analogs. [Figure 4, in particular.] Miller et al. also teaches the use of carbamoyl group to link the lipid-polyalkylamine conjugate. [Figure 5, in particular.] In the instant case, Miller et al. teaches a composition comprising cholesterol carbamoyl spermine and its analogs.

[3] Jorgensen et al. U.S. PreGrant Pub. No. 2002/0188023 A1, published December 12, 2002.

Miller et al. did not teach the use of ceramide as the lipid. However, at the time the invention was made, Jorgensen et al. teaches the use of ceramide as an alternative lipid to cholesterol. [Paragraph 0064, in particular.] Jorgensen et al. establishes that cholesterol and ceramide can be used in place of each other, art recognized equivalents. Therefore, it would have been prima facie obvious for one of ordinary skill in the art to use ceramide as the lipid in the lipid-polyalkylamine conjugate of Miller et al. In the instant case, both Miller et al. and Jorgensen et al. teach that lipid-polyalkylamine compound is a cationic liposome that can be used to facilitate delivery of therapeutic agents such as DNA, mRNA, antisense oligonucleotides, proteins and drugs into cells—all of which are biologically active molecules that modulates and induces the immune response. Additionally, the use of ceramide in place of cholesterol renders the compound of Miller et al. as ceramide carbamoyl-spermine (CCS). One of ordinary skill in the art would have been motivated to do to make a composition that facilitates delivery of therapeutic agents. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of one lipid for another, art recognized equivalents, is routinely practiced in the art.

Neither Miller et al. nor Jorgensen et al. not include a biologically active molecule with the composition. However, as noted above, both teach that the compound is a cationic liposome that can be used to facilitate delivery of therapeutic agents such as DNA, mRNA, antisense oligonucleotides, proteins and drugs into cells—all of which are biologically active molecules that modulates and induces the immune response. Thus,

at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to include a biologically active molecule, including those derived from the influenza virus with the lipid-polyalkylamine conjugate. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate delivery of molecules, including those derived from the influenza virus to stimulate an immune response. One of ordinary skill in the art would have had a reasonable expectation of success for doing so because both references disclose that lipid-polyalkylamine conjugates are effective to facilitate delivery of drugs into cells.

Additionally, it would have been prima facie obvious for one of ordinary skill in the art to also include an immunostimulating agent, such as an adjuvant to the composition rendered obvious by Miller et al. and Jorgensen et al. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to stimulate the immune response induced by the composition rendered obvious by Jorgensen et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the use of adjuvants with therapeutic agents such as biologically active molecules is routinely practiced in the art.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/EMILY M LE/
Primary Examiner, Art Unit 1648

/E. M. L./
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